LETTERS TO THE EDITOR

Ciprofloxacin resistant *Neisseria gonorrhoeae*

Treatment failure with ciprofloxacin has been reported for isolates with MIC's $\geqslant$ 0·05 mg/l.[1] The mechanism of quinolone resistance in gonococci has recently been shown to be due to mutations in the *gyr*A gene analagous to the mutations that occur in *Escherichia coli* and *Staphylococcus aureus*[2] suggesting that there is potential for very high levels of ciprofloxacin resistance in gonococci. We describe two unrelated cases of ciprofloxacin resistant gonococcal infection occurring in the first six months of 1995: the first case was associated with the development of symptoms following treatment with ciprofloxacin; and the second exhibited extremely high level ciprofloxacin resistance (MIC 16 mg/l) similar to the levels of resistance found in *Enterobacteriaceae*.

A 41 year old caucasian man presented to the genitourinary medicine (GUM) department complaining of spots on his penis. He denied any symptoms of urethral discharge or dysuria. Ten days previously he had had unprotected intercourse with a casual sexual partner in Brazil. On examination, there were two erythematous macules on the glans penis and no evidence of urethral discharge. Routine microscopy of a urethral smear demonstrated the presence of greater than 20 pus cells per high power field and gram negative diplococci, both intra and extra cellularly. A urine specimen was clear on inspection. A presumptive diagnosis of gonorrhoea was made and he was treated with ciprofloxacin 250 mg orally as a stat dose, followed by oxytetracycline 250 mg four times daily for seven days. The diagnosis was subsequently confirmed by urethral and throat culture; urethral chlamydial ELISA, VDRL and TPHA tests and Hepatitis BsAg were all negative. After counselling, he elected to have an HIV test deferred for three months.

When reviewed 14 days later, he had four days previously developed a purulent urethral discharge, although no associated dysuria. He stated that he had completed the course of oxytetracycline, and had not had any intercourse. On examination a profuse urethral discharge was noted and a 2-glass urine test demonstrated a turbid first aliquot with a clear second. Microscopy and culture were again positive for *N gonorrhoeae*. He was treated with spectinomycin 2 g im and the symptoms resolved within one day of treatment, with clinical and microbiological cure at review one and two weeks later. The pre- and post-treatment isolates were forwarded to the Scottish *Neisseria gonorrhoeae* Reference Laboratory (SNGRL) for typing and susceptibility testing. Both isolates were microbiologically similar: they were non-penicillinase producers of serovar IB3, auxotype PA, resistant to ciprofloxacin (MIC 0·125 mg/l) and tetracycline (MIC 2·0 mg/l), of intermediate sensitivity to penicillin (MIC 0·50 mg/l) and cefuroxime (MIC 1·0 mg/l), but fully sensitive to erythromycin (MIC 0·50 mg/l) and spectinomycin (MIC < 16 mg/l). No other IB3/PA strains have been isolated in Scotland this year supporting the epidemiological data which suggests that the infection was acquired abroad (Brazil).

The development of a symptomatic infection following unsuccessful treatment of an asymptomatic infection may have resulted from the growth of large numbers of ciprofloxacin resistant bacteria from a mixed pre-treatment population which comprised both susceptible and resistant variants.

The second case involved a 21 year old Caucasian woman who presented to the GUM department with a contact slip from her husband who had been diagnosed as having gonorrhoea at a military hospital in England. She denied any other contacts in the previous three years. She had noticed an increase in vaginal discharge over the previous two weeks but had attributed this to the fact that she was 27 weeks pregnant. On examination, a thick mucopurulent vaginal discharge was noted. Characteristic gram negative diplococci were not noted on microscopy of vaginal, cervical or urethral smears, but epidemiological treatment with a seven day course of amoxycillin was instituted at her initial attendance. *N gonorrhoeae* was cultured from the urethra, endocervix and rectum and we were notified that the strain was penicillinase producing prior to full antibiotic sensitivities being available. By liaising with the referring clinic it was ascertained that her husband's gonococcal strain was also resistant to ciprofloxacin. In view of the multiple antibiotic resistance, and the patient's pregnancy, she was treated with spectinomycin 2 g im. Repeat gonococcal cultures one and two weeks later were all negative.

The isolate was forwarded to the SNGRL and confirmed as a PPNG isolate of serovar IB1, auxotype non requiring, resistant to ciprofloxacin (MIC 16 mg/l), of intermediate sensitivity to cefuroxime (MIC 0·50 mg/l), tetracycline (MIC 1·0 mg/l), erythromycin (MIC 2·00 mg/l), but fully sensitive to spectinomycin (MIC < 16 mg/l). The isolate carried a 3·05 MDa resistance plasmid as well as the 24·5 MDa transfer and 2·6 MDa cryptic plasmids.

Overall the prevalence of ciprofloxacin resistance (defined by an MIC > 0·05 mg/l) is low in Scotland and was found in only 1·3% (25/1960) of all isolates tested by the SNGRL between 1991 and 1994. The prevalence of ciprofloxacin resistance for the serovars described in this report was 1·6% (2/123) for IB3 (both non-PPNG isolates) and 8·5% (11/130) for IB1 (7 PPNG isolates). The actual level of ciprofloxacin resistance also tended to be low: the MIC of the 25 strains were 0·064 mg/l (4 strains); 0·125 mg/l (6 strains); 0·25 mg/l (7 strains); 0·50 mg/l (7

strains), and 2·0 mg/l (1 strain). The level of ciprofloxacin resistance (16 mg/l) in Case 2 is exceptionally high although the same level of resistance was previously found in a serovar IB3, auxotype PA, PPNG strain isolated in Liverpool from a patient who had acquired his infection in Spain.[3]

These cases highlight the importance of importation of ciprofloxacin resistant strains which should be taken into account in selection of therapy for patients who may have acquired their infections outwith the UK or in areas with a high level of penicillin resistant gonococci. In Japan, where fluoroquinolones have been widely used as first-line therapy for gonorrhoea for several years the decrease in the susceptibility of gonococci to quinolones has been so rapid that fluoroquinolone resistance in gonorrhoea may be a new worldwide problem complicating the treatment of gonococcal infections.[4]

C THOMPSON
Department of Genitourinary Medicine, Victoria Hospital, Kirkcaldy, Fife, UK
H YOUNG
A MOYES
Scottish Neisseria gonorrhoeae Reference Lab, Department of Medical Microbiology, Edinburgh University Medical School, Edinburgh EH8 9AG, UK

Address correspondence to: Dr C Thompson.

1 Jephcott AE, Turner A. Ciprofloxacin resistance in gonococci. *Lancet* 1990;335:165.
2 Kumamoto Y, Nishimura M, Hirosel T, Yoshida H, Derluchi K. Analysis of resistance mutation of DNA gyrase in *Neisseria gonorrhoeae* resistance to new quinolone antibacterial agents. Abstract. IUVDT World STD/AIDS Congress, Singapore 1995.
3 Birley H, Mcdonald P, Carey P, Fletcher J. High level ciprofloxacin resistance in *Neisseria gonorrhoeae*. *Genitourin Med* 1994;70:292–3.
4 Tanaka M, Kumazawa J, Matsumoto T, Kobayashi I. High prevalence of *Neisseria gonorrhoeae* strains with reduced susceptibility to fluoroquinolones in Japan. *Genitourin Med* 1994;70:90–3.

Accpeted for publication 12 September 1995.

Prevalence of antibodies to HIV-1 and HIV-2 in women attending a sexually transmitted disease clinic in Luanda, Angola

North and East Angola border on countries such as Congo, Zaire and Zambia that show a high incidence of AIDS. In these regions, as in most African countries, the spread of HIV is mainly via the heterosexual route and is more prevalent in urban areas than in the rural ones. At present few data are available on HIV viruses spread in Angola.[1 2]

In order to depict the diffusion of HIV-1 and HIV-2 infections in an urban area of Angola, we performed a retrospective survey on 400 females attending the outpatient clinic of *Maternidade Lucrecia Paim* in Luanda during July and August 1992 and presenting with symptoms of sexually transmitted diseases. Patients were submitted to gynaecological examination and blood sample collection. The presence of vaginal or cervical ulcers was found in 51 out of 400 women (12·75%). Sera from blood samples were submitted to HIV-1 and HIV-2 ELISA (Murex). Nineteen out of 400 (4·75%) showed a positive or equivocal result. These sera were further assayed by Western blot (Diagnostic Biotechnology) kit to detect the pattern of antibodies against HIV-1 and HIV-2 (table). Eight out of 19 sera showed a typical HIV-1 pattern, the others were negative (3/19) or indeterminate (8/19). None out of eight HIV-1 positive samples met the criteria for HIV-2 positivity (presence of 2 anti env antibodies) when assayed by HIV-2 Western blot, but most of them were positive for the HIV-2 core proteins. Among the three sera negative for HIV-1 antibodies, two evidenced antibodies against both p26 and gp41 and one against p26 HIV-2 proteins. The eight indeterminate sera showing a single antibody against core (6/8) or pol (1/8) or env (1/8) HIV-1 proteins, were also indeterminate for HIV-2 tests showing the presence of p26 (6/8) or both p26 and gp41 (2/8) HIV-2 proteins. The presence of at least one antibody against HIV-2 in all sera submitted to Western blot remains to be clarified since the anomaly in testing African sera has been reported.[3] All indeterminate sera were further analysed by Western blot for antibodies against HTLV-1 and HTLV-2. A slight reactivity to core proteins were highlighted in three sera only.

Our data indicate that four out of eight (50%) HIV-1 positive women showed vaginal or cervical ulcers, whereas among the indeterminate ones only four out of 14 (28%) showed vaginal or cervical ulcers. These ulcer prevalences are much higher than that found in the

Western blot (WB) assay on ELISA HIV-1 and 2 positive sera, and presence of vaginal and cervical ulcers in a study population of 400 women in Luanda, Angola

Patient	*Ulcers*	*HIV-1 WB*	*HIV-1 WB*	*HIV-2 WB*	*HIV-2 WB*
1	+	IND	GP160	IND	P26
2	+	NEG		IND	P26
3	−	POS	Full pattern	IND	P53,P26,P16
4	+	POS	Full pattern	IND	P26
5	+	POS	Full pattern	IND	NEG
6	−	IND	P55	IND	GP41,P26
7	+	POS	Full pattern	IND	P26
8	+	POS	Full pattern	IND	P26
9	−	POS	Full pattern	IND	P68,P26
10	−	NEG		IND	GP41,P26
11	−	POS	Full pattern	IND	P68,P26,P16
12	−	IND	P31	IND	P26
13	−	IND	P17	IND	P26
14	−	POS	Full pattern	IND	P26
15	+	IND	P55,P24	IND	P68,GP41,P26
16	−	IND	P24	IND	P68,P26
17	+	IND	P24	IND	P26
18	−	NEG		IND	GP41,P26
19	−	IND	P24	IND	P26